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# NEW THERAPEUTIC METHOD CONSISTING IN THE USE OF ORGANIC LIQUIDS EXTRACTED FROM GLANDS AND OTHER ORGANS.

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In 1869, at the Paris School of Medicine, I delivered several lectures, the principal object of which was to establish that all glands, with or without excretory ducts, give to the blood, by an internal secretion, principles which are of great importance if not necessary. I showed this to be the case particularly for the kidneys, the suprarenal capsules, and the sexual glands. Experiments I made in 1875 at Nahant (near Boston, U.S.) confirmed the correctness of the view I had advanced. I thought that if we could safely introduce the principle of the internal secretion of a gland taken from a living animal into the blood of men suffering from the lack of that secretion, important therapeutic effects would thereby be obtained. In February 1889, in a paper deposited at the Biological Society, I stated that I had found that means, and that it consisted in injecting under the skin the liquid extract we can get easily from glands by pressure, with the addition of a little water. Since then, with the help of my assistant, Professor d'Arsonval, I have pushed matters considerably forward, and I have especially tried to prove that not only glands, but all tissues, have, besides their influence on blood resulting from the interchange of nutrition, an internal secretion.<sup>1</sup>

Since then facts of great importance have accumulated, and the new therapeutic method has not only received demonstrations of its value from persons acting consciously under its principles in acknowledging them, but also from others who acted as if they themselves had discovered those principles.

I will give a short statement of facts and views in ten or twelve parts, and I begin at once with what relates to the first.

**I. Innocuity of Injections of Organic Liquid Extracts under the Skin and in Veins.**—Experiments made by Wooldridge, Foa and Pallavicini, Ewald, Bouchard, Langendorff, H. Roger, and others, had shown that there is great danger in introducing under the skin or directly into the blood liquids extracted from the thymus, the thyroid, the testicles, the brain, the liver, the kidney, the suprarenal capsules. This is only partly true, even when the injection is made without proper filtration, but the numerous experiments made by d'Arsonval and myself have positively established the perfect innocuity of large proportions of liquid organic extracts injected under the skin or in the veins or arteries, after they have been submitted to filtration in the principal of the sterilising and filtering apparatuses of d'Arsonval. We have tried over and over again liquids from all the organs above named, and also from the pancreas, the spleen, the medulla of bones, the lymphatic glands, the spinal cord, the lungs, the heart and other muscles, and also pieces of the digestive canal. The only effects of an infusion of these liquids into blood vessels which were temporarily bad were those of the over-fullness of the circulatory apparatus, when the quantity injected was large, and it was so with any liquid extract, no difference in that respect existing between an injection of the various extracts and that of serum, natural or artificial. We found that all the organic liquids have a useful tonic effect, some of them, however, in a much more marked manner than others.

**II. Modes of Introduction of the Various Organic Liquid Extracts into the Blood.**—Now that it has been ascertained that the active principles of the thyroid gland are not destroyed

as are the toxic principles of woorara, of serpents' venom, etc., it has been asked in many quarters if the various organic extracts, or rather pieces of the various organs, could not be swallowed and their action obtained after absorption in the digestive tube. Dr. Ch. Macalister has shown that thymus and the medulla of bone can have their therapeutic action like the thyroid after having been swallowed. It may be that a number of other organs or tissues will be like the three just named. It is not so, however, for the sexual glands; it is not so for the pancreas; and we must, therefore, think of other means of introducing the organic principles of these glands and of some other parts into the blood. A good many persons, under my advice, have made use of the process of introducing into the rectum an extremely condensed liquid extract of the gland to be used. If it is the male sexual glands, the two taken from a guinea-pig are finely minced, then crushed, and after addition of a little water the whole is thrown on a paper filter. The bowels having been washed by an enema, the whole amount of filtered liquid (about 30 or 40 grammes) is injected in the rectum, which usually keeps it. There is a rather rapid absorption, and the effect produced is almost as good as that of an injection of a considerably smaller amount of the same liquid injected under the skin. This mode of introduction into the system of any organic liquid can certainly be used with profit. It is not so powerful as can be an injection under the skin. Still, it can do much, as Dr. Frémy obtained with it a considerable amelioration of all symptoms in a case of leprosy treated by him under my supervision.

As regards injections, either under the skin or into the blood, they are too well known for my speaking of them. A most important means, which unfortunately requires a very skilful hand, has been used by Dr. de La Jarrige, who injects the organic liquids into the lungs through the laryngeal glottis. Absorption there is almost immediate. There is no pain, no coughing, no trouble of any kind. It is assuredly the very best and safest way of injecting the 2, 4, 6, or 8 grammes of organic liquid which we wish to introduce into the blood, provided, however, that the medical man then acting is sufficiently adroit for that delicate operation.

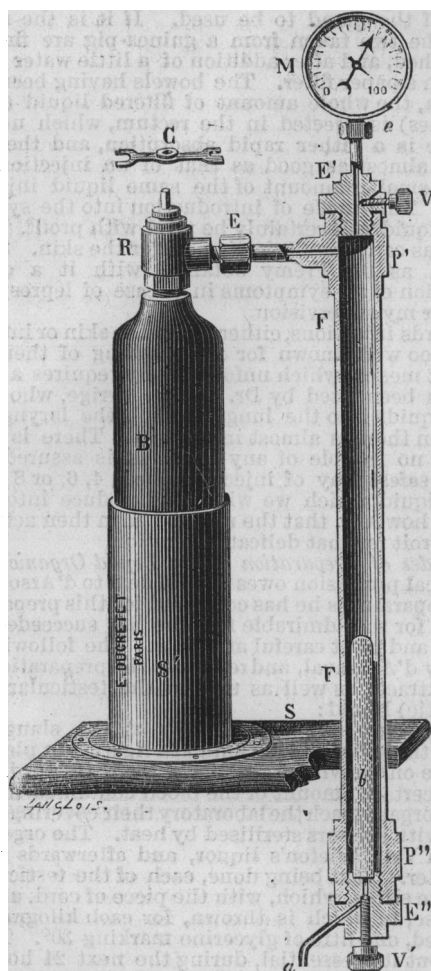
**III. Modes of Preparation of the Liquid Organic Extracts.**—The medical profession owes a great deal to d'Arsonval for the various apparatuses he has contrived for this preparation, and especially for the admirable filter he has succeeded to obtain after long and most careful attempts. The following is from a paper by d'Arsonval, and relates to the preparation of all the organic extracts, as well as that of the testicular (which we call orchitic) liquid:

1. We procure testicles of bulls at the slaughter-house. Just after the killing of the animal a ligature is placed as high as possible on the whole mass of the spermatic cord, so as to get at least a certain amount of the blood contained in the veins. When the organs reach the laboratory their coverings are at once cut away with scissors sterilised by heat. The organs are then washed in Van Swieten's liquor, and afterwards in recently boiled water. That being done, each of the testicles is cut in four or five slices, which, with the piece of cord, are placed in a glass vase, in which is thrown, for each kilogramme of the organs used, one litre of glycerine marking 30°. The vase is covered, but it is essential, during the next 24 hours, to turn over a good many times the slices and other pieces of organs. At the end of that period an addition of 500 cubic centimetres of freshly boiled water, containing 25 grammes of pure chloride of sodium, is made. The liquid so obtained is then made to pass through a paper filter (we use the syrup grey filter No. 8 of the Laurent series). Before doing this, however, we hardly need to say that the paper filter and the glass funnel in which it is placed must be thoroughly washed with boiling water. The filtered liquid is slightly rose-coloured. To hasten the filtration it is well to raise the temperature of the glyceric solution to 40° C. (104° F.); the viscosity is thereby suppressed.

2. Of the various means we have made use of to obtain a liquid absolutely free from microbes or other dangerous pieces of solid matter, the most important is the one we will now describe. The sterilising d'Arsonval filter, represented in the annexed figure, is composed of a metallic hollow cylinder s', which receives and keeps immovable the thick steel bottle B, filled with liquid carbonic acid; a metallic

<sup>1</sup> I will refer to the first papers of d'Arsonval and I have published together. They are in the volume of 1891 of the *Comptes Rendus de la Société de Biologie*, Avril 18, p. 248; Avril 26, p. 265; Juillet 4, p. 535; Octobre 24, p. 722; and in *Archives de Physiologie*, Paris, 1891, July 1st.

tube, *FF*, which has borne the weight of 200 atmospheres; a metallic stopper screwed on the lower extremity of this tube, and carrying the filtration bougie *b*. This bougie is of a kind of clay, in which kaolin is replaced by pure alumina; it is fixed on the metallic stopper by an indiarubber tube, which is made to press most tightly on the bougie and the metal. A screwing top, *v*, is attached to the metallic stopper, and by it we can at will close or open the apparatus. When it is opened, the liquid which has passed inside of the filter *b* runs out through the tube *a*. The top of the tube *FF* is closed by a metallic stopper *v*, which is surmounted by a manometer graduated up to 100 atmospheres, and carries also a screwing tap, which allows the escape of the accumulated carbonic gas



when this escape is needed. An adjoining lateral tube, *x*, serves for communication between the sterilising filter and the liquid carbonic acid contained in the steel bottle *B*. A stopper, *x*, with a steel point, put in action by a key, *c*, gives the possibility of establishing or stopping communication between the two tubes *B* and *FF*, so that the pressure against the liquid which is to be filtered may be gradual. The two tubes or two apparatuses form a whole, fixed on a wooden tablet, *s*, which is screwed firmly on a table. To sterilise the glyceric liquid it is first thrown into the tube *FF*; then, after having screwed solidly the superior stopper on which is the manometer *M*, and having turned to the end the closing screws *v* and *v'*, the tap *x* of the steel bottle *B* is opened. The carbonic acid enters rapidly into the tube *FF*, and presses over the liquid. A pressure of 50 to 60 atmospheres is maintained for about an hour, during which all the microbes that may be present are crushed and killed. The pressure may be in-

creased, notably if the apparatus is submitted to a temperature of 40° C. (104° F.). Neither the albumoids nor the soluble ferments are in the least altered, as has been ascertained with pancreas and yeast. When the sterilisation is considered sufficient (from half to one hour for tissues of a healthy animal), the tap *v'* is opened, and the liquid filters rapidly through the bougie *b*, after having been submitted to two sterilisations, the first one by CO<sub>2</sub> under pressure, the second by the filtration.

IV. *Importance of Injections of Renal Liquid in Organic Affections of the Kidneys.*—In 1869 I gave many reasons to show that the phenomena of uræmia are only partly due to the accumulation of certain substances in the blood. I tried to show that when the kidneys are disorganised and their internal secretion stopped or considerably diminished the absence of certain principles furnished by that secretion is a great cause also of the uræmic phenomena. Much later on (in June, 1889) these views were laid before the Société de Biologie.<sup>2</sup> Since then, either alone or with d'Arsonval (who also had experimented alone), a good many experiments were made on rabbits and guinea-pigs, showing that life lasted much longer after the extirpation of the two kidneys (sometimes one day, one and a-half, and even two days) when injections of renal liquid were made. The details of these decisive experiments will soon be published in my Journal.

The study of the phenomena of anuria leads forcibly to the view that the internal secretion of the kidney is of the greatest importance. Very frequently in those cases—existing generally when the kidneys are not disorganised or when there is but one of them considerably disorganised—there is no uræmic phenomenon showing itself for seven, eight, or ten days—a period of tolerance which clearly shows that the accumulation of urea and other principles of the urine in the blood is not the principal cause of uræmia. It is certainly not correct to look upon a vicarious urination by the skin and mucous membranes as explaining the innocuity of a complete cessation of secretion of urine for so many days, as in most cases on record (there are plenty in Merklen's excellent work, *Etude sur l'Anurie*, Paris, 1881, and in Labadie-Lagrave's big work, *Urologie Clinique des Maladies des Reins*, Paris, 1888) there was hardly any appearance of a vicarious urination.

The mode of death in cases of anuria, when the internal secretion continues, even when the kidneys are in a good part diseased<sup>3</sup> (as in the most important case of Sir James Paget in the *Transactions of the Clinical Society*, 1869, vol. ii, p. 17), is very different from that of cases of disorganisation of the kidneys when the internal secretion is stopped. There is much less violence at the time of death and before it in anuria than in Bright's disease, in nephritis, and other kinds of disorganisation of the kidneys.

All that I know of the physiology and diseases of these organs clearly shows the paramount importance of their internal secretion, the cessation of which is notably more to be dreaded than is the cessation of the external secretion. This, of course, naturally leads to the trial of the renal liquid in subcutaneous injections<sup>4</sup> in cases of organic disease of the kidneys. The experiments made by D'Arsonval and myself render it almost certain that good effects would be obtained in that way.

A case of uræmia, in which Professor Dieulafoy has injected the renal liquid, supports the correctness of this view. Although the patient in that case soon died, he was revived sufficiently to show the benefit of the injection.

V. *Importance of Injections of the Liquid Extract of Pancreas in Cases of Diabetes.*—The discovery of Von Mering and Minkowski that diabetes will appear in dogs if the whole of the pancreas has been removed has been the subject of most interesting researches in France by Hédon, Thiroloix, Gley, Lépine, and Chauveau and Kaufmann. That the pancreas, like the testicles, the ovaries, the kidneys, has an internal

<sup>2</sup> See *Comptes Rendus de la S. de B.*, p. 421.

<sup>3</sup> No trouble appears when a small part of the thyroid is left after thyroidectomy, and no diabetes occurs when a small part of the pancreas remains in cases of extirpation of that gland. In such circumstances the internal secretion by a small part is enough to prevent the bad effects due to a complete arrest of the internal secretion.

<sup>4</sup> Of course, what we know of the success obtained by patients having taken pieces of thyroid, of thymus, and of medulla of bone by the mouth leads to the importance of making trials of the action of pieces of raw kidney taken also by the mouth.

secretion, which is even more important than its external one, there cannot be a doubt now. It is, therefore, quite natural that many practitioners have tried the pancreatic liquid extract against diabetes, and especially that peculiar form of it which has long ago been shown by Lancereaux to depend on a disease of the pancreas.

What theory indicated has proved correct in a good measure; injections of the pancreatic liquid have been useful, but no case of cure, to my knowledge, has been recorded. In a case of Dr. Rémond, the azoturia (which is excessive, as well shown by Hédon in cases of absence of the pancreatic internal secretion), became very much better under the influence of injections of the liquid extract of pancreas. Another organic liquid has gone further, and some cures have been obtained, the first of all in the case of a Calcutta Hindu who came to me, and whom I sent to my friend Dr. W. D. Waterhouse, of West Hampstead. That other organic extract is the orchitic liquid, which has considerably more power against any form of diabetes than the pancreatic liquid. I have for some time already recommended the simultaneous use of those two liquids in all cases of glycosuria.

VI. *The Liver possesses also an Internal Secretion, and the Hepatic Liquid Extract might be sometimes Used with Profit.*—The well-known physiological facts relating to the production of sugar, and still more of glycogen, positively show already that that gland has an internal secretion. But has it any other, and especially does it give to the blood principles the absence of which, when the liver is considerably disorganised, produces serious and peculiar symptoms? There are very good reasons to think so, and it is most likely that in many cases of diffuse organic disease of the liver a number of the symptoms depend on the lack of the internal secretion. Unfortunately in mammals there is no conclusion to be drawn relating to that point when we take away the liver or only tie all its blood vessels. In frogs, however, experiments I made long ago, repeated lately by Dr. H. Roger, show that the taking away of the liver is a rapid cause of death after tonic or clonic convulsions. This clearly shows the importance of the internal secretion of the gland.

Certainly it would be well to make use of the hepatic liquid in cases of extensive organic disease of the liver, whether it causes jaundice or not.

[To be continued.]

## ON THE TREATMENT OF BRONCHIECTASIS.

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For many years I have taken a special interest in the subject of bronchiectasis, having met with a series of cases during the time that I was pathologist and extra-physician to the Royal Infirmary, which seemed to me to support a theory of the disease different from that which had been generally accepted. The generally accepted theory then was, and to a large extent still is, that the dilatations are produced by the contraction of fibrous tissue in the lungs, and in dense adhesions connecting the lungs with the thoracic wall. This was the view maintained by Sir Dominic Corrigan.

Now, my cases seemed to show that while dilatations do certainly occur, as Corrigan supposed, in cases of fibroid phthisis, that process does not explain many, and indeed the most typical, examples of the disease. For bronchiectasis is often present when there is no cirrhosis, and in not a few instances the fibroid change follows upon it as a secondary consequence. I, therefore, maintained that an atrophic process in the walls of bronchial tubes affords the real explanation, and that, given such an atrophy, the pressure of the air in the respiratory tract leads to the opening out of the tubes, while, as a further consequence, accumulation and decomposition of the mucus necessarily follows, and this gives rise to further anatomical changes in the mucous and other coats of the bronchi, and in the surrounding pulmonary

tissue, and explains the great clinical features of the malady. To this accumulation and decomposition are due the fœtor of the breath and the sputum, and the peculiar attacks of coughing as local results, and the occasional febrile attacks and general disturbance of the system as results of the absorption of the poisonous products of decomposition.

My observations during the twenty-six years which have elapsed since I wrote upon this subject<sup>1</sup> have confirmed the views which were then expressed, and in accordance with this I have been striving to find remedies which might be useful. It was clear enough that we have little in our power in the way of preventing the occurrence of the atrophy, and that except by keeping down cough, so far as that might be warrantable, we could but slightly interfere with the pressure conditions which tend to dilate the weakened walls. But on the other hand, the constant aim has been to prevent decomposition of the sputum and its consequences. And this we have sought to do in many ways. The administration of turpentine, creasote, carbolic acid, salol, and other antiseptics by the stomach, making the patient live in an atmosphere saturated with volatile antiseptic substances, directing sprays and vapour of various kinds into the air passages, have all been sedulously tried with greater or less, but on the whole a very limited and temporary, advantage.

During the past winter I have adopted a plan which has proved eminently satisfactory in the one case in which I have tried it. It consists in the intratracheal injection of menthol and guaiacol with olive oil. The proportions which we used were: Menthol, 10 parts; guaiacol, 2 parts; olive oil, 88 parts. Of this a drachm was injected into the trachea twice daily. The result was a speedy diminution and disappearance of the fœtor, with improvement in all respects.

The patient, J. M., a surfaceman, aged 34, was admitted to Ward 22 on December 5th, 1892, complaining of bronchitis with fœtor of breath. His family history was good, and he had been quite healthy until two years ago, when he had disease of the mastoid cells, and was successfully treated in the surgical wards by Mr. Millis. On leaving the hospital he caught cold, and was unable to throw it off. Soon after it set in he and his companions observed that his breath had become offensive, and that on coughing he brought up a quantity of foul-smelling yellow mucus. These symptoms continued, and gradually became more severe, while he became subject to occasional feverish attacks and exacerbations of cold, and his strength failed.

On admission he was very ill; thin, emaciated, flushed about the cheeks, with a dirty complexion and an oily appearance of skin. His temperature, which was 102° on admission, rose to 103.4° when he had been for a short time in bed, and his expression was very anxious. His breath was very offensive, and he was expectorating large quantities of intensely foetid sputum, which, in spite of carbolic acid being placed in the dish and its vapour freely disengaged on each side of his bed, permeated the whole ward and the vestibule leading to it. On examination his alimentary system was found to be badly deranged, his phlegm foul, his appetite and digestion much impaired, and his bowels constipated.

The hæmopoietic system showed no special change.

The circulatory showed rapid and rather feeble action of the heart, but no evidence of organic change in it or in the vessels.

The respiratory system was much affected. There was considerable dyspnoea and frequent cough. The fits of coughing were peculiarly prolonged, and at first resultless, but ultimately attended by the discharge of a large quantity of grey-greenish-yellow expectoration with an oily look, and the most repulsive fœtor.

On microscopic examination the sputum showed large numbers of pus cells, oil globules, fatty crystals, and on one occasion some fragments of pulmonary elastic tissue, but no tubercle bacilli. The chest was fairly well formed: the percussion note anteriorly was clear throughout; posteriorly at and below the position at the root of the lungs the note was altered, being in some parts dull, in others high pitched and tympanic. This was especially marked on the left side. On auscultation the ordinary signs of bronchitis were audible at almost every point on both lungs, but near the inferior angles of the scapulae behind, the breathing was at several points cavernous, and accompanied by numerous crepitations, fine, medium, coarse, and bubbling *râles*; the vocal resonance being at these points pectoriloquous. Towards the apices and the extreme bases there was no evidence of consolidation.

Excepting for the dusky colour and oiliness, the skin was natural. The urinary, nervous, and locomotory systems showed no changes except those proper to the feverish condition.

The history of the case, as well as the characters of the sputum, made it clear that the fœtor was not due to pulmonary gangrene, and the physical signs made it certain that vomicæ existed in the lung; these vomicæ might have been phthisical or bronchiectatic. That they were not due to phthisis was clear from their position, from the long-standing fœtor, from the characters of the sputum itself, and in particular the absence of the tubercle bacilli, while in all respects both the symptoms and signs corresponded to those of bronchiectasis.

<sup>1</sup> *Edinburgh Medical Journal*, July, 1867.